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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,998	05/02/2006	Vincent Cool	05-1083	3592

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MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DRIVE
32ND FLOOR
CHICAGO, IL 60606

EXAMINER	
NIEBAUER, RONALD T	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
10/22/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/562,998	**Applicant(s)** COOL ET AL.	
	Examiner RONALD T. NIEBAUER	**Art Unit** 1654	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 19 October 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Ronald T Niebauer/
Examiner, Art Unit 1654

/Anish Gupta/
Primary Examiner, Art Unit 1654

Continuation of 11. does NOT place the application in condition for allowance because: Applicants provide arguments related to the outstanding 103 rejection. Applicants have not amended or cancelled any of the claims.
Applicants argue that a portion of the Rink reference relates to a method of making a support resin not to a procedure for conducting solid-state peptide synthesis.
Applicants argue that the preferred bases are tertiary or secondary amines not quaternary amines and thus Rink teach away.
Applicants argue that benzyltrimethylammonium hydroxide might be too strong for use in peptide synthesis and could cause undesirable reactions.
Applicants argue that Mihala teaches away since Mihala teaches best results with a salt that is not claimed.
Applicants argue that Mihala uses a solvent system that is excluded from the claims and Mihala teach that certain peptides are insoluble in DMF,NMP, and DMSO.
Applicants argue that the teachings of Merrifield are not relevant as Merrifield does not teach the reaction as in the instant claims and the peptide includes a group that is not an amino acid.

Applicants arguments have been fully considered but are not found persuasive.
Although Applicants argue that a portion of the Rink reference relates to a method of making a support resin not to a procedure for conducting solid-state peptide synthesis, such portion of Rink (column 5 lines 2-5) expressly relates to removal of an amino protecting group - i.e. removal of W from NH-W. It is noted that claim 3a expressly refers to cleaving an amino group. In addition to carrying out such removal to make a resin, Rink also teach such procedure for peptide synthesis (column 8 lines 24-51).
Although Applicants argue that the preferred bases are tertiary or secondary amines not quaternary amines and thus Rink teach away, it is noted that MPEP section 2123 II states: "Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971).....Furthermore, “[t]he prior art’s mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed....” In re Fulton, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004)". In the instant case, the prior art does not criticize or discredit the use of quaternary amines. On the contrary, Rink teach advantages of using such - Rink expressly teach that the use of benzyltrimethylammonium hydroxide for cleavage can be carried out at lower temperatures and can be concluded after a much shorter reaction time (column 5 lines 22-25).
Although Applicants argue that benzyltrimethylammonium hydroxide might be too strong for use in peptide synthesis and could cause undesirable reactions, MPEP 2145 I states “An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness.” In the instant case, there is no factual evidence that benzyltrimethylammonium hydroxide might be too strong for use in peptide synthesis and could cause undesirable reactions.
Although Applicants argue that Mihala teaches away since Mihala teaches best results with a salt that is not claimed, it is noted that the instant rejection is a multiple reference 103 rejection and as such any single reference does not necessarily anticipate the claims. Further, Mihala does not criticize or discredit (see MPEP 2123 II) the use of benzyltrimethylammonium hydroxide. Importantly, Mihala teach that the tetrabutyl ammonium salt additive is used to enhance solubility (page 567 first complete paragraph). Mihala teach that the tetrabutyl ammonium salt additive lead to improved efficiency (title, abstract, Table 1). Mihala suggests that use of the ammonium salt as an additive provides an alternative for improving coupling efficiency in solid phase peptide synthesis (last paragraph page 567).
Although Applicants argue that Mihala uses a solvent system that is excluded from the claims and Mihala teach that certain peptides are insoluble in DMF,NMP, and DMSO; first it is noted that that Mihala recite that the art recognizes a wide variety of solvents including DMF, NMP, DMSO, TFE-DCM (page 565 first column). Thus Mihala recognizes the use of more than just chloroform-phenol. Further, Mihala refer to (page 565) solution peptide synthesis when using the maximum protecting strategy of Sakakibara that it may happen that fully protected Boc-peptides may be insoluble in DMF,NMP, or DMSO. However, such statement is with respect to solution peptide synthesis. Rink Mihala and Merrifield all teach the well-known solid phase peptide synthesis technique. Further, such statement refers to the maximum protecting strategy of Sakakibara and there is no evidence that Rink use such strategy. Further, Mihala only state that insolubility 'may' occur withing giving more specifics. Such generalization which is applied to a different synthesis strategy is not adequate to deter one from using salts in solid phase peptide synthesis as taught by Rink Mihala and Merrifield.
Although Applicants argue that the teachings of Merrifield are not relevant as Merrifield does not teach the reaction as in the instant claims and the peptide includes a group that is not an amino acid, it is noted that the instant rejection is a multiple reference 103 rejection and as such any single reference does not necessarily anticipate the claims. Further, Merrifield teach acylation which is a step that can be performed during peptide synthesis. The instant claims recite 'comprising' and are thus open to additional steps. In summary, Rink Mihala and Merrifield all teach the well-known solid phase peptide synthesis technique. The references teach advantages of including salts specifically ammonium salts at various stages of the process. Rink teach (column 5 lines 7-25, column 8 lines 24-51) that benzyltrimethylammonium hydroxide can be used to remove the amino protecting group. Rink expressly teach that when benzyltrimethylammonium hydroxide is used that the cleavage can be carried out at lower temperatures and can be concluded after a much shorter reaction time. Merrifield also teach the use of benzyltrimethylammonium hydroxide, specifically during the addition step to enable the chemical reaction (page 1293 section ‘acylation’). Further, Mihala addresses the problem of aggregation by using an ammonium salt to increase solubility and decrease aggregation. Since the references show that the art recognizes the use of ammonium salts as additives at various stages of the peptide synthesis process one would have a reasonable expectation of success.
For these reasons and the reasons set forth previously, Claims 3-8,12-14,16,19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rink (US 5,004,781) and Mihala et al (Journal of Peptide Science ‘An alternative solid phase peptide fragment condensation protocol with improved efficiency’ 7:565-568 (2001), cited in previous office action) and Merrifield et al (J Org Chem ‘The limits of reaction of radioactive dicyclohexylcarbodiimide with amino groups during solid-phase peptide synthesis' v42 (1977) pages 1291-1295) and Finger (US 4,218,400).
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